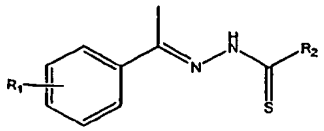
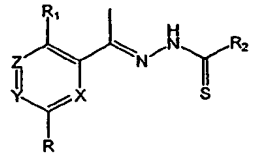
FIG. 1



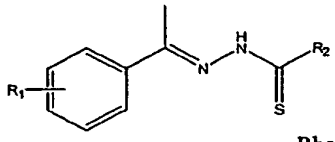
Cmpd#	R1	R2	Cruzain IC50 (μM)	*T.cruzi* Survival (days @ 5μM)	Host Toxicity
1a	2'-phenyl	NH_2	>20	5 days	none
1b	3'-phenyl	NH_2	8	43 days	none
1c	4'-phenyl	NH_2	5	8 days	toxic
2a	2'-NH-phenyl	NH_2	>20	5 days	none
2b	3'-NH-phenyl	NH_2	>20	43 days	none
2c	4'-NH-phenyl	NH_2	>20	43 days	none
2d	3'-O-phenyl	NH_2	10	27 days	toxic
2e	4'-O-phenyl	NH_2	10	28 days	toxic
3d	3'-Br	NH_2	0.06	43 days	none
3e	3'NH_2	NH_2	>20	5 days	none
3f	2'-OH	NH_2	>20	5 days	none
3g	3'-OH	NH_2	>20	5 days	none
3h	4'-OH	SMe	>20	5 days	none
4a	3'-Br	Shit	>20	7 days	toxic
4c	3'-Br	piperidyl	5	5 days	none
4d	3'-Br	N-methylpiperazinyl	5	14 days	toxic
4e	3'-Br	NEt_2	5	5 days	none

FIG. 2



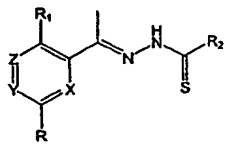
Cmpd#	R	R1	R2	X	Y	Z	Cruzain IC50(μM)	*T.cruzi* Survival (days @5μM)	Host Toxicity
3a	H	H	NH_2	N	CH	CH	>20	43 days	none
3b	H	H	NH_2	CH	N	CH	>20	5 days	none
3c	H	H	NH_2	CH	CH	N	>20	5 days	none
4b	H	H	SMe	N	CH	CH	>20	5 days	none
3i	CH(Me)NNHC(S)NH_2	H	NH_2	CH	CH	CH	5	5 days	none
3j	CH(Me)NNHC(S)NH_2	H	NH_2	N	CH	CH	>20	5 days	none
3k	CH(Me)NNHC(S)NH_2	Me	NH_2	CH	CMe	N	>20	5 days	none

FIG. 3



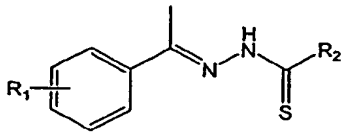
Cmpd#	R1	R2	Rhodesain IC50(μM)	*T.brucei* ED50 (μM)
1a	2'-phenyl	NH_2	>20	>20
1b	3'-phenyl	NH_2	1.1	12
1c	4'-phenyl	NH_2	0.09	10
2a	2'-NH-phenyl	NH_2	>20	>20
2b	3'-NH-phenyl	NH_2	0.8	8
2c	4'-NH-phenyl	NH_2	18	4.5
2d	3'-O-phenyl	NH_2	0.55	6
2e	4'-O-phenyl	NH_2	8	3
3d	3'-Br	NH_2	0.05	>20
3e	3'NH_2	NH_2	>20	>20
3f	2'-OH	NH_2	>20	>20
3g	3'-OH	NH_2	>20	>20
3h	4'-OH	NH_2	>20	>20
4a	3'-Br	SMe	>20	10
4c	3'-Br	piperidyl	4	3
4d	3'-Br	N-methylpiperazinyl	4	2
4e	3'-Br	NEt_2	1.8	3

FIG. 4



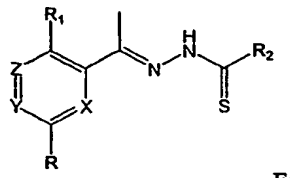
Cmpd#	R	R1	R2	X	Y	Z	Rhodesain IC50(μM)	T.brucei ED50 (μM)
3a	H	H	NH_2	N	CH	CH	>20	4
3b	H	H	NH_2	CH	N	CH	>20	>20
3c	H	H	NH_2	CH	CH	N	>20	>20
4b	H	H	SMe	N	CH	CH	>20	0.3
3i	CH(Me)NNHC(S)NH_2	H	NH_2	CH	CH	CH	0.33	>20
3j	CH(Me)NNHC(S)NH_2	H	NH_2	N	CH	CH	>20	>20
3k	CH(Me)NNHC(S)NH_2	Me	NH_2	CH	CMe	N	>20	>20

FIG. 5



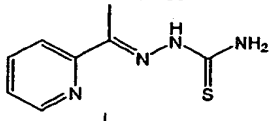
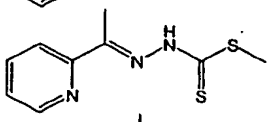
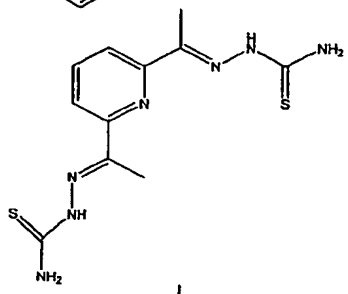
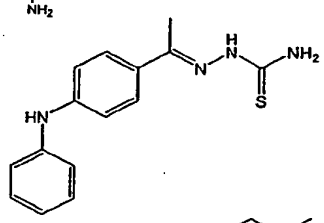
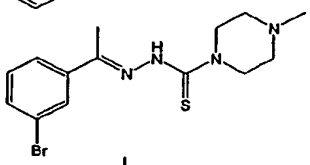
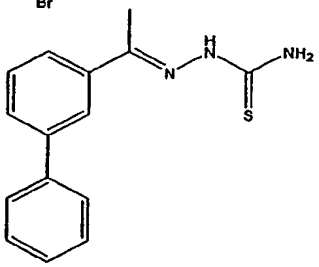
Cmpd#	R1	R2	Falcipain 2 IC50(μM)	*P.falciparum* ED50(μM)
1a	2'-phenyl	NH_2	>20	>20
1b	3'-phenyl	NH_2	>20	>20
1c	4'-phenyt	NH_2	10	>20
2a	2'-NH-phenyl	NF_2	>20	>20
2b	3'-NH-phenyl	NH_2	>20	>20
2c	4'-NH-phenyl	NH_2	>20	9.9
2d	3'-O-phenyl	Nm_2	>20	>20
2e	4'-O-phenyl	NH_2	>20	>20
3d	3'-Br	NH_2	>20	>20
3e	3'NM_2	NH_2	>20	>20
3f	2'-OH	NH_2	>20	>20
3g	3'-OH	NH_2	>20	>20
3h	4'-OH	NH_2	>20	>20
4a	3'-Br	SMe	>20	>20
4c	3'-Br	piperidyl	>20	20
4d	3'-Br	N-methylpiperazinyl	>20	4
4e	3'-Br	NEt_2	>20	>20

FIG. 6



Cmpd#	R	R1	R2	X	Y	Z	Falcipain 2 IC50(μm)	P. falciparum ED50(μm)
3a	H	H	NH_2	N	CH	CH	>20	0.08
3b	H	H	NH_2	CHN		CH	>20	>20
3c	H	H	NH_2	CHCH		N	>20	>20
4b	H	H	SMe	N	CH	CH	>20	0.03
31	CH(Me)NNHC(S)NH_2H	NH_2		CHCH		CH	>20	>20
3j	CH(Me)NNHC(S)NH_2K	NH_2		N	CH	CH	>20	0.03
3k	CH(Me)NNHC(S)NH_2Me	NH_2		CHCMeN			>20	>20

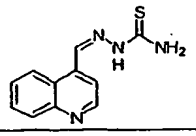
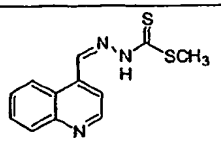
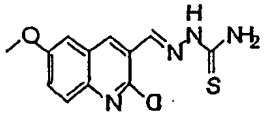
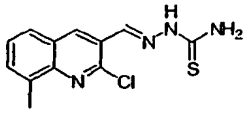
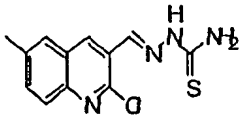
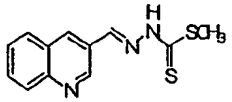
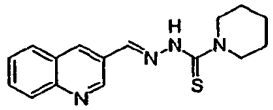
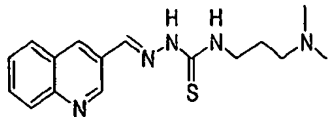
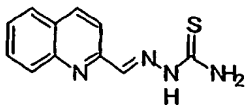
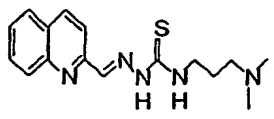
FIG. 7

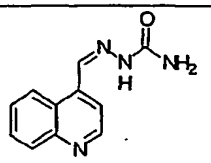
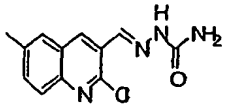
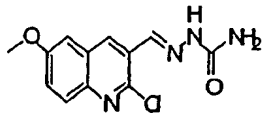
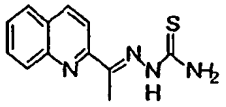
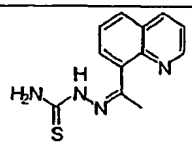
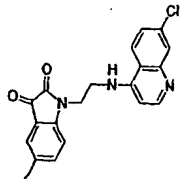
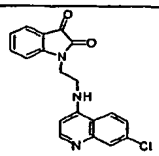
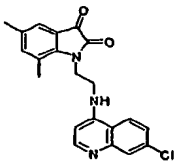
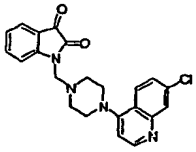
Compound	Structure	Survival (toxicity) 5 mgs/kg weight	20mgs/kg weight
3a		20 hours (*)	62 hours (**)
4b		62 hours (No)	62 hours (No)
3j		62 hours (No)	62 hours (No)
2c		62 hours (No)	62 hours (No)
4d		62 hours (No)	62 hours (No)
1b		62 hours (No)	62 hours (No)

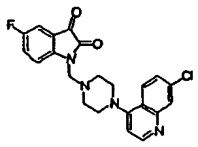
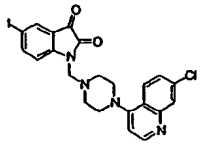
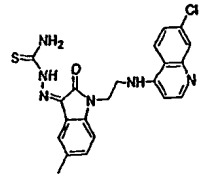
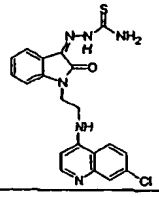
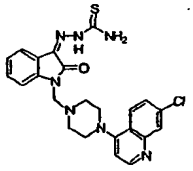
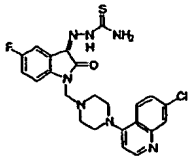
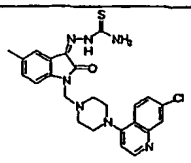
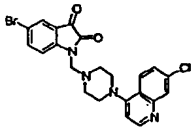
*Animal suffered toxic shock after injection, characterization by tremor, loss of mobility, malaise, and death

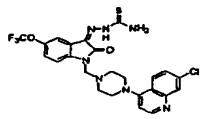
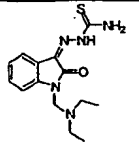
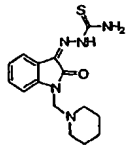
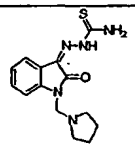
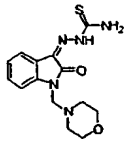
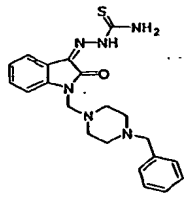
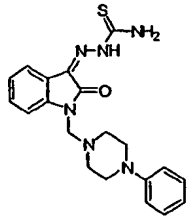
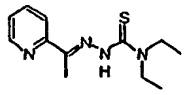
**Animal survived treatment with malaise, loss of mobility and ruffled hair after injection

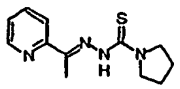
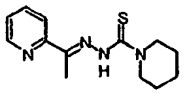
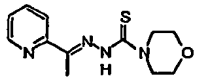
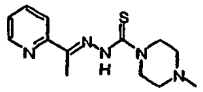
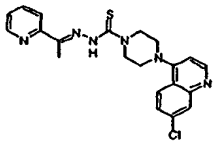
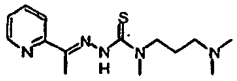
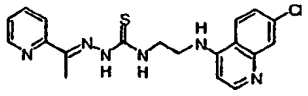
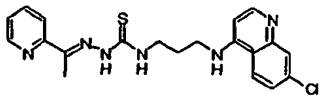
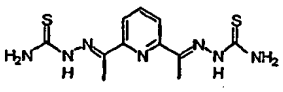
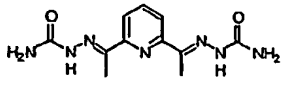
FIG. 8

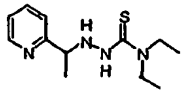
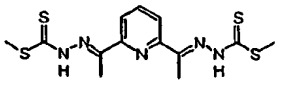
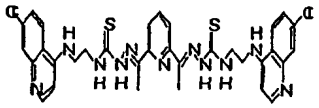
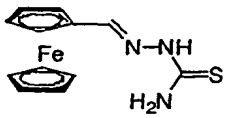
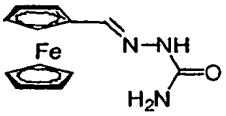
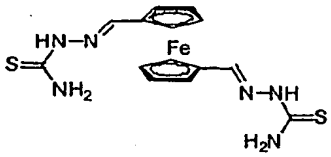
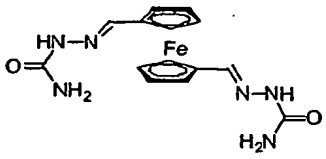
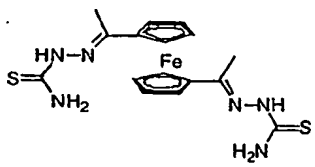
Structure	Cruzain IC50 (μM)	Rhodesain IC50 (μM)	P. falciparum W2 IC50 (μM)
	1.5	0.4	>20
	>10	>10	>20
	>10	9	>20
	0.312	5	>20
	>10	not determined (ND)	>20
	>10	>10	>20
	>10	>10	>20
	>10	>10	3.3
	>10	5	>20
	>10	>10	7.7

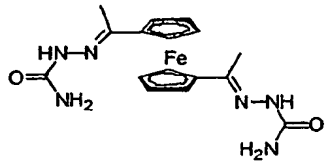
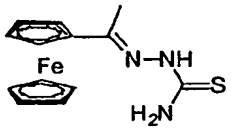
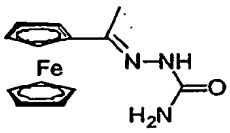
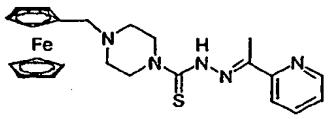
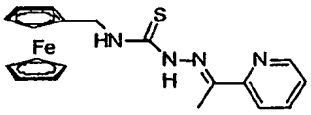
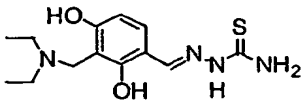
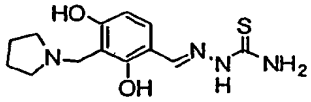
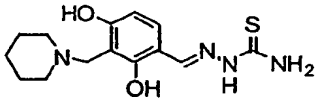
Structure	Cruzain IC50 (μM)	Rhodesain IC50 (μM)	P. falciparum W2 IC50 (μM)
	>10	>10	>20
	>10	>10	>20
	>10	>10	>20
	5	0.8	2.5
	>10	ND	>20
	>10	>10	0.489
	>10	>10	0.125
	>10	>10	0.227
	>10	>10	0.961

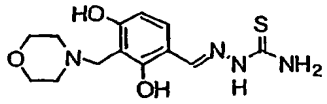
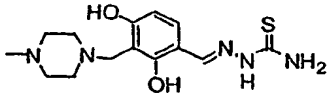
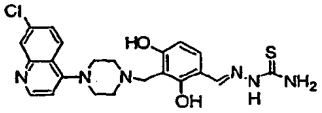
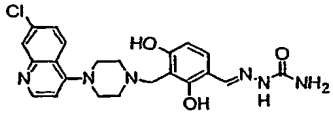
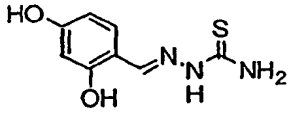
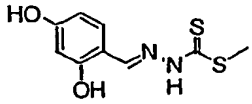
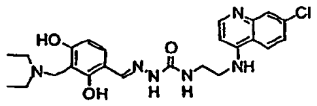
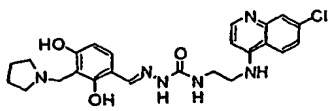
Structure	Cruzain IC50 (μM)	Rhodesain IC50 (μM)	P. falciparum W2 IC50 (μM)
	>10	>10	0.908
	>10	>10	0.794
	2	4	0.051
	ND	ND	0.242
	>10	8	0.957
	*ND*	*4*	*1.193*
	*ND*	*3*	*1.809*
	*ND*	*1*	*1.226*

Structure	Cruzain IC50 (μM)	Rhodesain IC50 (μM)	P. falciparum W2 IC50 (μM)
	ND	5	0.833
	ND	ND	>20
	ND	ND	>20
	ND	ND	>20
	ND	ND	>20
	ND	ND	>20
	ND	ND	>20
	ND	4	0.025

Structure	Cruzain IC50 (μM)	Rhodesain IC50 (μM)	P. falciparum W2 IC50 (μM)
	1.8	0.11	0.008
	1.6	4	0.028
	ND	ND	0.013
	ND	0.7	0.013
	ND	ND	0.212
	ND	1.8	0.26
	ND	0.42	0.212
	ND	ND	0.19
	ND	4	6.521
	ND	5.5	0.14

Structure	Cruzain IC50 (μM)	Rhodesain IC50 (μM)	P. falciparum W2 IC50 (μM)
	>10	ND	0.032
	1.5	0.3	1.677
	0.8	0.4	0.054
	8.5	ND	>20
	ND	ND	>20
	3.5	4.2	>20
	ND	ND	>20
	2	1.8	>20

Structure	Cruzain IC50 (μM)	Rhodesain IC50 (μM)	P. falciparum W2 IC50 (μM)
	ND	ND	>20
	>10	10	>20
	ND	ND	>20
	ND	ND	0.0246
	ND	ND	0.0161
	9	4	>20
	2.1	2	>20
	5	3	>20

Structure	Cruzain IC50 (μM)	Rhodesain IC50 (μM)	P. falciparum W2 IC50 (μM)
	20	10	>20
	ND	7	>20
	ND	1	0.376
	ND	>10	0.246
	ND	ND	>20
	ND	ND	>20
	ND	5	0.437
	2.8	2.5	1.065

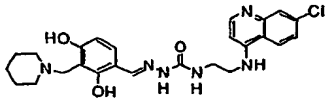
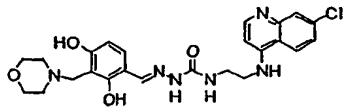
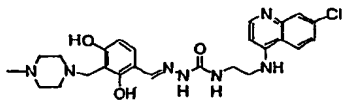
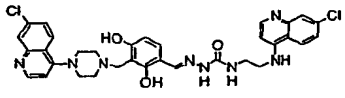
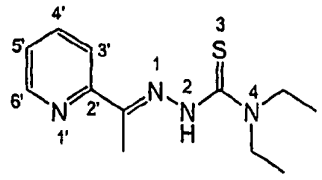
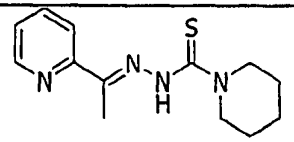
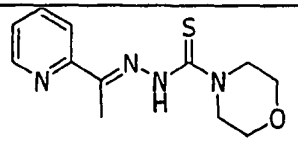
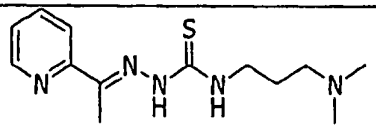
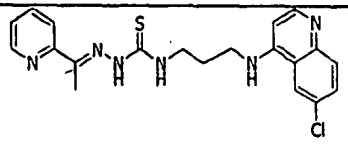
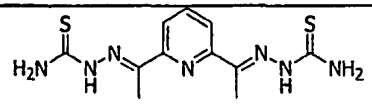
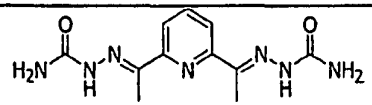
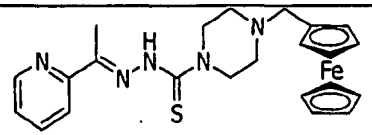
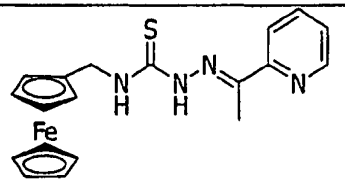
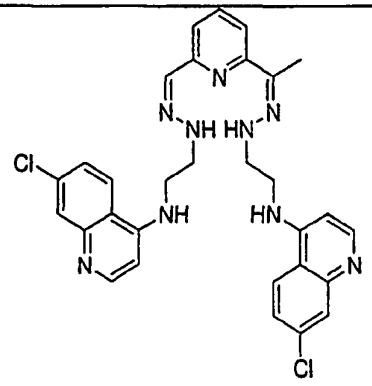
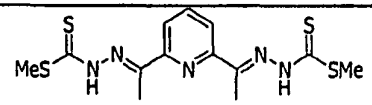
Structure	Cruzain IC50 (μM)	Rhodesain IC50 (μM)	P. falciparum W2 IC50 (μM)
	1.8	1.8	0.265
	>10	>10	0.113
	ND	ND	0.376
	3.5	ND	0.077

FIG. 9

Compound Structure	Compound		% inhibition T. brucei			ED_{50} µg/ml		Cytotoxicity	Therapeutic
	ID	30	10	3	1	+/- 95% CL	repeat	ED_{50} µg/ml	Index
	MC 156	98.24	98.85	99.57	99.67	<1.11 ®	0.0384 ± 0.0004	0.04	1
	MC 158	98.76	99.22	99.68	99.73	<1.11 ®	0.0015 ± 0.0005	0.3	200
	MC 159	97.78	100	100	98.51	<1.11 ®	0.265 ± 0.66	1.8	7
	MC 162	100	100	99.95	98.45	<1.11 ®	0.0014 ± 0.0005	13.5	9643
	MC 164	99.72	99.54	99.52	99.39	<1.11 ®	0.019 ± 0.009	10	526

Compound Structure	Compound		% inhibition T. brucei			ED_{50} µg/ml		Cytotoxicity	Therapeutic
	ID	30	10	3	1	+/- 95% CL	repeat	ED_{50} µg/ml	Index
	MC 172	15.25	12.89	10.09	7.3	>30		>300	-
	MC 172B	99.84	99.09	99.23	94.85	<1.11 ®	0.552 ± 0.156	>300	-
	MC 176	99.23	99.25	98.27	82.42	<1.11 ®	1.331 ± 0.045	0.57	0
	MC 177	100	99.87	99.92	99.78	<1.11 ®	0.0537 ± 0.004	3.08	57
	MC 184	97.82	98.31	98.46	98.74	<1.11 ®	0.0009 ± 0.0005	18.2	20222
	MC 186	99.44	99.76	99.74	98.73	<1.11 ®	0.0182 ± 0.0012	2.9	159